d his

L1   2212 S IN SILICO
L2   3 S L1 AND ((PROTEIN OR PEPTIDE) AND (REDUCE? IMMUNOGEN?))
L3   0 S L1 AND ((PROTEIN OR PEPTIDE) AND (IMMUNOGENECITY))
L4   8 S L1 AND ((PROTEIN OR PEPTIDE) AND (IMMUNOGEN?))
L5   5 S L4 NOT L2

=> d l4 bib,abs 1-8

L4   ANSWER 1 OF 8   CAPLUS   COPYRIGHT 2003 ACS
AN   2002:908189   CAPLUS
DN   138:185948
TI   Search for potential vaccine candidate open reading frames in the Bacillus
      anthracis virulence plasmid pXO1: in silico and in vitro
      screening
AU   Ariel, N.; Zvi, A.; Grosfeld, H.; Gat, O.; Inbar, Y.; Velan, B.; Cohen,
      S.; Shafferman, A.
CS   Department of Biochemistry and Molecular Genetics, Israel Institute for
      Biological Research, Ness Ziona, 74100, Israel
SO   Infection and Immunity (2002), 70(12), 6817-6827
      CODEN: INFIBR; ISSN: 0019-9567
PB   American Society for Microbiology
DT   Journal
LA   English
AB   A genomic anal. of the Bacillus anthracis virulence plasmid pXO1, aimed at
      identifying potential vaccine candidates and virulence-related genes, was
      carried out. The 143 previously defined open reading frames (ORFs) were
      subjected to extensive sequence similarity searches (with the nonredundant
      and unfinished microbial genome databases), as well as motif, cellular
      location, and domain analyses. A comparative genomics anal. was conducted
      with the related genomes of Bacillus subtilis, Bacillus halodurans, and
      Bacillus cereus and the pBtoxis plasmid of Bacillus thuringiensis var.
      israeliensis. As a result, the percentage of ORFs with clues about their
      functions increased from .apprx.30% (as previously reported) to more than
      60%. The bioinformatics anal. permitted identification of novel genes
      with putative relevance for pathogenesis and virulence. Based on our
      analyses, 11 putative proteins were chosen as targets for
      functional genomics studies. A rapid and efficient functional screening
      method was developed, in which PCR-amplified full-length linear DNA
      products of the selected ORFs were transcribed and directly translated in
      vitro and their immunogenicities were assessed on the basis of
      their reactivities with hyperimmune anti-B. anthracis antisera. Of the 11
      ORFs selected for anal., 9 were successfully expressed as full-length
      polypeptides, and 3 of these were found to be antigenic and to have
      immunogenic potential. The latter ORFs are currently being
      evaluated to det. their vaccine potential.
RE.CNT 69   THERE ARE 69 CITED REFERENCES AVAILABLE FOR THIS RECORD
                ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4   ANSWER 2 OF 8   CAPLUS   COPYRIGHT 2003 ACS
AN   2002:889930   CAPLUS
TI   Rationally engineered proteins or antibodies with absent or
      reduced immunogenicity
AU   Tangri, S.; LiCalsi, C.; Sidney, J.; Sette, A.
CS   Epimmune Incorporated, San Diego, CA, 92121, USA
SO   Current Medicinal Chemistry (2002), 9(24), 2191-2199
      CODEN: CMCHE7; ISSN: 0929-8673
PB   Bentham Science Publishers
DT   Journal
LA   English

AB   One challenge assocd. with the clin. use of **protein** therapeutics
     destined for chronic administration is the potential for the development
     of unwanted anti-drug immune reactions. The mol. basis for this
     reactivity is the binding of **peptide** fragments (epitopes)
     derived from the breakdown of the **protein** drug to the HLA
     receptors expressed by the patient's immune cells. If these epitopes are
     recognized as "foreign" by the immune system, specific helper T
     lymphocytes (HTL), are activated, which initiate and direct the formation
     of antibodies against the **protein** drug. These antibodies can
     bind and neutralize the **protein** drug, resulting in either
     decreased efficacy or total ineffectiveness of the drug. Moreover,
     various safety concerns, such as allergic reactions and other adverse
     events, are also frequently assocd. with the formation of anti-drug
     antibodies. Herein, we describe the development of "ImmunoStealth", an
     integrated bioinformatics, biochem. and cellular immunol. approach that
     specifically addresses the issue of unwanted immune responses against
     protein therapeutics. Unwanted HTL epitopes are identified using
     in **silico** sequence anal. methods and high throughput in vitro
     biochem. evaluations and thereafter confirmed using cellular
     immunogenicity assays. The "offending" epitopes within the drug
     are then rationally modified to alter their HLA binding capacity, and thus
     render them non-recognizable by the immune system. This technol. will
     ultimately facilitate the design of safer, more potent and more economical
     drugs.
RE.CNT 77   THERE ARE 77 CITED REFERENCES AVAILABLE FOR THIS RECORD
              ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4   ANSWER 3 OF 8 CAPLUS COPYRIGHT 2003 ACS
AN   2002:832831 CAPLUS
DN   137:351519
TI   Modified human interferon .alpha. with reduced **immunogenicity**
     for therapeutic uses
IN   Carr, Francis J.; Carter, Graham; Jones, Tim; Baker, Matthew; Watkins,
     John; Hanlon, Marian
PA   Merck Patent G.m.b.H., Germany
SO   PCT Int. Appl., 76 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002085941	A2	20021031	WO 2002-EP2218	20020301

     W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
         CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
         GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
         LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
         PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
         UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU,
         TJ, TM
     RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,
         CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
         BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
PRAI EP 2001-105088   A   20010302
AB   The present invention relates to polypeptides to be administered esp. to
     humans and in particular for therapeutic use. The polypeptides are
     modified polypeptides whereby the modification results in a reduced
     propensity for the polypeptide to elicit an immune response upon
     administration to the human subject. The invention in particular to the
     modification of human interferon alpha and specifically interferon .alpha.
     2 (INF.alpha.2) to result in **proteins** that are substantially
     non-**immunogenic** or less **immunogenic** than any
     non-modified counterpart when use in vivo.

AN   2002:814284   CAPLUS
DN   137:309486
TI   Surface **proteins** and their genes of Streptococcus pyogenes and
      their use for treatment of infections caused by .beta.-hemolytic
      streptococci
IN   Olmstead, Stephen Bruce; Zagursky, Robert John; Nickbarg, Elliott Bruce;
      Winter, Laurie Anne
PA   Wyeth, John and Brother Ltd., USA
SO   PCT Int. Appl., 109 pp.
      CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002083859	A2	20021024	WO 2002-US11610	20020412

```
      W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
          CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
          GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
          LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
          PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA,
          UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
      RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,
          CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
          BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
```

PRAI US 2001-283358P   P   20010413
AB   The present invention provides nucleic acid and **protein** compns.
      and methods to ameliorate and prevent infections caused by all
      .beta.-hemolytic streptococci, including groups A, B, C, and G.   To
      identify polynucleotides and polypeptides useful for the amelioration and
      prevention of infections caused by .beta.-hemolytic streptococci, two
      strategies, a genomic approach and a proteomic approach, were used to
      identify surface-localized Streptococcus pyogenes **proteins**.   The
      genomic approach included an extensive genomic anal. in **silico**
      of the S. pyogenes genome using several algorithms design to identify and
      characterize genes that would encode surface-localized **proteins**.
      Some of the **proteins** are also characterized for opsonphagocytic
      activity.   The polynucleotides, polypeptides, and antibodies of the
      invention can be formulated for use as **immunogenic** compns.   Also
      disclosed are methods for immunizing against and reducing .beta.-hemolytic
      streptococcal infection, and for detecting .beta.-hemolytic streptococci
      in a biol. sample.   The present invention claims a total of 668 sequences,
      but the Sequence Listing was not made available on publication of this
      patent application.

AN   2002:696124   CAPLUS
DN   137:226946
TI   Modified ciliary neurotrophic factor (CNTF) with reduced
      immunogenicity by removing its T cell epitopes
IN   Carr, Francis J.; Carter, Graham
PA   Merck Patent Gmbh, Germany
SO   PCT Int. Appl., 33 pp.
      CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002070698	A2	20020912	WO 2002-EP2084	20020227

```
      W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
          CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
          GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
```

```
            LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL,
            PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG,
            US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
        RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,
            CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
            BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
```

PRAI EP 2001-105089   A   20010302

AB   The present invention relates to polypeptides to be administered esp. to
     humans and in particular for therapeutic use. The polypeptides are
     modified polypeptides whereby the modification results in a reduced
     propensity for the polypeptide to elicit an immune response upon
     administration to the human subject. The invention in particular relates
     to the modification of human ciliary neurotrophic factor (CNTF) to result
     in CNTF **proteins** that are substantially non-**immunogenic**
     or less **immunogenic** than any non-modified counterpart when used
     in vivo. 81 13-Amino acid T cell epitopes of human CNTF are identified
     and subjected to modification assisted by in **silico** modeling
     techniques to reduce or remove nos. of potential T-cell epitopes in CNTF
     for drug design. Various amino acid residues for substituting the crit.
     residues in these T cell epitopes are listed. DNA sequences coding for
     the modified **proteins**, pharmaceutical compns. contg. the
     modified **proteins**, and a method of manuf. of the
     proteins are also claimed but NOT provided.

L4   ANSWER 6 OF 8 CAPLUS COPYRIGHT 2003 ACS
AN   2001:785109 CAPLUS
DN   136:322902
TI   T-helper cell-response to MHC class II-binding **peptides** of the
     renal cell carcinoma-associated antigen RAGE-1
AU   Stassar, Marike J. J. G.; Raddrizzani, Laura; Hammer, Jurgen; Zoller,
     Margot
CS   Department of Tumor Progression and Immune Defense, German Cancer Research
     Center (DKFZ), Heidelberg, Germany
SO   Immunobiology (2001), 203(5), 743-755
     CODEN: IMMND4; ISSN: 0171-2985
PB   Urban & Fischer Verlag
DT   Journal
LA   English
AB   Recently, epitope prediction software for HLA-DR binding sequences has
     become available. In view of the importance of T helper (Th) cell
     activation in immunotherapy of cancer and evidences supporting
     immunogenicity of renal cell carcinoma (RCC), we have tested 4
     peptides of RAGE-1 binding promiscuously to HLA-DR mols. for
     induction of an immune response. The **peptides** predicted by the
     TEPITOPE program using a stringent threshold were derived from the open
     reading frame 2 and 5 of RAGE-1. Induction of response was evaluated by
     culturing peripheral blood mononuclear cells (PBMC) in the presence of
     peptide-loaded dendritic cells (DC) to det. proliferative activity
     and cytokine expression. Two out of 5 donors did not respond to any of
     the 4 **peptides**, 2 donors responded to one **peptide** and
     one donor responded to two other **peptides**. Notably, as revealed
     by blocking studies and T cell subtype definition, **peptides**
     bound to MHC class II mols. and **peptide** pulsed DC exclusively
     activated CD4+ T cells, which were of the Th1 subtype. With respect to
     clin. application it is important that (un)responsiveness of individual
     donors' PBMC was a very consistent feature. Though we have not tested
     explicitly whether these **peptides** correspond to naturally
     processed **peptides**, the possibility to define those patients
     whose Th might respond to in **silico** predicted **peptides**
     of RAGE-1, by an in vitro assay, could well be a helpful step towards
     setting up a RAGE-1 based immunotherapeutic protocol.
RE.CNT 50   THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD
              ALL CITATIONS AVAILABLE IN THE RE FORMAT

AN   2001:209260   CAPLUS
DN   135:342702
TI   HLAMatchmaker: a molecularly based donor selection algorithm for highly
      alloimmunized patients
AU   Duquesnoy, R. J.
CS   CLSI Tissue Typing Laboratory, Division of Transplantation Pathology,
      University of Pittsburgh Medical Center, Thomas E. Starzl Transplantation
      Institute, Pittsburgh, PA, USA
SO   Transplantation Proceedings (2001), 33(1-2), 493-497
      CODEN: TRPPA8; ISSN: 0041-1345
PB   Elsevier Science Inc.
DT   Journal; General Review
LA   English
AB   A review with refs., describes an alternative strategy for identifying
      potential donors for highly sensitized patients. HLAMatchmaker is an
      easy-to-use computer-based algorithm that addresses amino acid sequence
      polymorphism as crit. components of **immunogenic** epitopes that
      can elicit alloantibodies. This "in **silico**" compatibility test
      allows detn. of the structural basis of an HLA antigen mismatch. The
      review also discusses amino acid triplet polymorphisms in
      antibody-accessible sites of HLA class I mols.; detn. of HLA compatibility
      at the amino acid triplet level; anal. of serum reactivity patterns and
      identification of acceptable HLA antigen mismatches; and relative
      immunogenicity of HLA triplets.
RE.CNT 7   THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
                ALL CITATIONS AVAILABLE IN THE RE FORMAT

AN   2000:525163   CAPLUS
DN   133:236572
TI   Characterization of a monoclonal antibody, D73H, that maps to a highly
      conserved region on fibrinogen B.beta. chain
AU   Rybarczyk, B. J.; Pereira, M.; Simpson-Haidaris, P. J.
CS   Department of Pathology, Medicine-Vascular, University of Rochester School
      of Medicine and Dentistry, Rochester, NY, USA
SO   Thrombosis and Haemostasis (2000), 84(1), 43-48
      CODEN: THHADQ; ISSN: 0340-6245
PB   F. K. Schattauer Verlagsgesellschaft mbH
DT   Journal
LA   English
AB   The primary structure of fibrinogen is highly conserved across species,
      yet often times monoclonal antibodies produced against the fibrinogen of
      one species will not crossreact with the fibrinogen of another. Herein,
      the authors describe the prodn. and characterization of murine MAb, D73H,
      raised against human fibrinogen. D73H cross-reacts with a highly
      conserved epitope on the B.beta. chain of fibrinogen from human, rat,
      bovine, guinea pig, and mouse. Western blotting revealed that D73H
      reacted with the B.beta. chain of plasmin fragment D, localizing its
      epitope to B.beta.134-461. A 7 kDa band was identified by D73H in Western
      blots of reduced fibrinogen CNBr-fragments. N-terminal sequencing mapped
      this fragment to B.beta.243-253, further localizing the epitope to
      B.beta.243-305. In **silico** anal. indicated that B.beta.243-305
      is predominantly hydrophilic, and surface probability prediction indicated
      three potential antigenic determinants corresponding to B.beta.252-258,
      B.beta.262-269, and B.beta.279-286. Further in **silico** anal. of
      the crystal structure of fibrinogen fragment D-D indicated that
      B.beta.262-269 (FGRKWDPY) is predominantly .alpha.-helical and located on
      the surface of the mol. adjacent to a bend imposed in the .beta. chain at
      residue 260, which is near the junction between the rigid coiled-coil
      domain and the globular C-terminus. A synthetic **peptide**
      corresponding to B.beta.261-272 competitively inhibited the binding of
      D73H to the B.beta. chain of denatured intact fibrinogen and reduced and
      denatured B.beta. chain in Western blots, exptl. proving the validity of

these predictive algorithms. Together these data indicate that, although plasmin resistant, B.beta. chain residues B.beta.261-272 comprising the D73H epitope are highly conserved across species, surface exposed, and **immunogenic**.

RE.CNT 38   THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD
              ALL CITATIONS AVAILABLE IN THE RE FORMAT